DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/3/08 has been entered.

Applicant's response filed 4/3/08 is acknowledged and has been entered.

The Declaration under 37 C.F.R. 1.132 of Inventors Dr. Jonathan Schneck and Dr. Mathias Oelke filed 4/3/08 is acknowledged and has been entered.

2. Applicant is reminded of Applicant's election with traverse of Group I and species of solid support that is a bead, a T lymphocyte affecting molecule that is an antibody that specifically binds to CD28, an MHC class I complex comprising at least two fusion proteins, wherein a first fusion protein comprises a first MHC class I alpha chain and a first Ig heavy chain and wherein a second fusion protein comprises a second MHC class I alpha chain and a second Ig heavy chain, wherein the first and second Ig heavy chains associate to form the MHC class I molecular complex, wherein the MHC class I molecular complex comprises a first MHC class I peptide binding cleft and a second MHC class I peptide binding cleft in Applicant's response filed 7/31/06. The Examiner notes that the currently pending claims do not recite "at least two fusion proteins" nor that the first and second Ig heavy chains associate to form the MHC class I molecular complex.

Claims 1, 12-15, 48 and 49 are currently being examined.

3. For the purpose of prior art rejections, the filing date of the instant claims 1, 12-15, 48 and 49 is deemed to be the filing date of the instant application, *i.e.*, 7/14/03, as the parent application serial no. 60/395,781 does not support the claimed limitations of the instant application.

Application serial no. 60/395,781 provides support for the limitations of a solid support that is a bead that has attached thereto, a co-stimulatory molecule that is an anti-CD28 antibody and an MHC class I molecule that consists of the extracellular regions of the MHC class I alpha chain as well as β2m, and wherein the MHC class I alpha chain extracellular regions are attached at the C-terminal end to Ig constant region comprising the hinge region, and wherein the MHC class I-Ig fusion proteins form dimers. It is noted by the Examiner that the instant claims encompass a rigid solid support that is a bead, said bead comprising an antibody that specifically binds to CD28, two fusion proteins, each of which may comprise an entire class I alpha chain and an entire

immunoglobulin heavy chain, two β2m polypeptides and two immunoglobulin light chains.

Application serial no. 60/395,781 does not provide support for the limitation wherein the fusion protein comprises an MHC class I alpha chain and an Ig heavy chain wherein the fusion protein comprises the entire MHC class I alpha chain and the entire Ig heavy chain, not just the extracellular regions or the Ig hinge and constant regions, respectively.

The Declaration under 37 C.F.R. 1.132 of Dr. Jonathan Schneck and Dr. Mathias Oelke filed 4/3/08 has been considered by the Examiner. The Examiner has found Applicant's arguments in the amendment filed 4/3/08 persuasive. The said arguments and the amendment of base claim 1 to delete reference to MHC class II complexes and to recite "two immunoglobulin light chains" have overcome the prior 103(a) rejections of record.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1, 12-15, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,268,411 B1 (of record) in view of Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

U.S. Patent No. 6,268,411 B1 discloses MHC class I/Ig divalent chimeric complexes chimeric complexes comprising two to four fusion proteins, each fusion protein comprising the extracellular regions of MHC class I α chain genetically fused to the variable region of an IgG1 heavy chain, and wherein the complexes further comprise β2m, Ig light chain and antigenic peptide bound in the MHC class I binding groove. U.S. Patent No. 6,268,411 B1 discloses that an identical antigenic peptide from a tumor associated antigen, a viral or infectious agent associated antigen, an autoimmune disease associated antigen, an alloantigen or xenogantigen, or an allergy associated antigen may be bound in the MHC molecule in the peptide binding groove. U.S. Patent No. 6,268,411 B1 discloses that the peptide/MHC/Ig complexes may be affixed to a solid substrate such as a glass or plastic slide or tissue culture plate or latex, PVC or polystyrene bead or a viral particle. U.S. Patent No. 6,268,411 B1 discloses that the viral particles that carry the complexes may also contain saline, a pharmaceutically acceptable carrier. U.S. Patent No. 6,268,411 B1 discloses that the peptide/MHC/ig complexes can be used to stimulate T cells, either *in vitro* such as for adoptive transfer or *in vivo*, and that immobilization of the said complexes can stimulate antigen specific T cells. U.S. Patent No. 6,268,411 B1 discloses that thus, these reagents can be used to selectively activate antigen specific T cells either *in vitro* or *in vivo* (especially abstract, Figure 1A, column 3 at lines 5-15, 30-64, column 8 at lines 9-27, column 9 at lines 24-67, column 10 at lines 12-67, column 11 at lines 1-62, column 16 at lines 55-67, claims).

U.S. Patent No. 6,268,411 B1 does not disclose that the bead comprising the MHC class I/Ig further comprises an anti-CD28 antibody.

Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08) teach co-immobilized (on a rigid solid support that is a plate) anti-CD28 antibodies along with class I/peptide complexes bound by anti-class I (anti-alpha 3) antibody, and use of the co-immobilized molecule to stimulate antigen-specific CD8+ T cells. Although Pardigon *et al* also teach stimulation of said T cells using each plate-bound molecule separately in series (MHC followed by anti-CD28) and also teach that signal 1 provided by MHC and signal 2 provided by anti-CD28 do not have to be delivered concomitantly to get optimal T cell activation, they teach sequential delivery in order to study the effect of such on potential situations encountered *in vivo* (see entire reference).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the rigid solid support disclosed by U.S. Patent No. 6,268,411 B1 to also include anti-CD28 antibodies as per the teaching of Pardigon *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a superior rigid solid support comprising an MHC complex that would be effective in stimulating CD8+ T cells *in vitro*.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have added a pharmaceutically acceptable carrier such as PBS to the solid substrate of the combined references.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to conveniently store the preparation.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1, 12-15, 48 and 49 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of U.S. Patent No. 6,268,411 B1 (IDS reference in the Form 1449 filed 7/14/03) in view of Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08).

Claims 1-34 of U.S. Patent No. 6,268,411 B1 are drawn to a composition comprising a complex comprising at least two chimeric proteins, wherein each chimeric protein comprises an MHC molecule, including an MHC class I alpha chain, and an Ig chain, including an Ig heavy chain that comprises a variable region, and wherein the complex further comprises immunoglobulin light chains and β2m, and an antigenic peptide bound to the amino terminus of β2m.

Claims 1-34 of U.S. Patent No. 6,268,411 B1 do not recite wherein the said composition is linked to a rigid solid support, nor wherein an antibody that binds CD28 is also linked to the rigid solid support.

Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08) teach co-immobilized (on a rigid solid support that is a plate) anti-CD28 antibodies along with class I/peptide complexes bound by anti-class I (anti-alpha 3) antibody, and use of the co-immobilized molecule to stimulate antigen-specific CD8+ T cells. Although Pardigon *et al* also teach stimulation of said T cells using each plate-bound molecule separately in series (MHC followed by anti-CD28) and also teach that signal 1 provided by MHC and signal 2 provided by anti-CD28 do not have to be delivered concomitantly to get optimal T cell activation, they teach sequential delivery in order to study the effect of such on potential situations encountered *in vivo* (see entire reference).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have attached the complexes recited in claims 1-34 of U.S. Patent No. 6,268,411 B1 to a rigid solid support and to also include anti-CD28 antibodies as per the teaching of Pardigon *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a superior solid substrate comprising an MHC complex that would be effective in stimulating CD8+ T cells *in vitro*.

8. Claims 1, 12-15, 48 and 49 are directed to an invention not patentably distinct from claims 1-104 of commonly assigned U.S. Patent No. 6,268,411 B1 in view of Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08) as enunciated above at item #7 of this Office Action.

9. The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 6,268,411 B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Eileen B. O'Hara, can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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